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Page 3 [Amendment Under 37 C.F.R. §1.116 to the July 18, 2000 Office Action - January 18, 2001]

455. (Amended) The oligo- or polydeoxyribonucleotide of claim 454, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide selfsignaling or self-indicating or self-detecting.

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459. (Amended) The oligo- or polydeoxyribonucleotide of claim 454, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the [alpha-position] α -position relative to the point of attachment to the nucleotide, a -CH2NH- moiety, or both.

461. (Amended) The oligo- or polydeoxyribonucleotide of claim 454, wherein said chemical linkage comprises or includes an olefinic bond at the [delta-position] $\underline{\alpha}$ position relative to the point of attachment to the nucleotide, or any of the moieties:

$$- CH = CH - CH_2 - NH -$$

$$[-CH = CH - CH_2 - O - CH_2 - CH - NH -,$$

- CH = CH₂ - NH -

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$$\begin{array}{c} 0 \\ || \\ - \ S \ -, \ - \ C \ - \ O, \ \text{and} \ - \ 0 \ - \ . \end{array}$$

466. (Amended) The oligo- or polydeoxyribonucleotide of claim 454, wherein Sig is selected from the group consisting of a ligand and a specific ligand binding protein [complexed with a binding protein therefor, and said binding protein is conjugated to ferritin].

476. (Amended) The composition of claim 474, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and [anti-Sig] anti-hapten immunoglobulin.

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480. (Amended) The oligo- or polydeoxyribonucleotide of claim 478, wherein the sugar moiety of said terminal nucleotide has [hydrogen] oxygen atoms at each of the 2' and 3' positions thereof.

482. (Amended) An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:

wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H- , HO- , a monophosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H- , HO- , a monophosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H-, HO-, a monophosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached [to x, y or z] directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y, z, and a combination thereof, said Sig [being a moiety capable of non-radioactive detection] comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to [x, y or z] said phosphate or when said modified nucleotide is incorporated into said oligo- or polydeoxynucleotide or when said oligo- or polydeoxynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

Claim 483, line 2, after "oligo or" and before "self-signaling" change "polynucleotide" to -- polydeoxyribonucleotide -- .

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487. (Amended) The oligo- or polydeoxyribonucleotide of claim 482, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the [alpha-position] α -position relative to the point of attachment to the nucleotide, a -CH₂NH- moiety, or both.

489. (Amended) The oligo- or polydeoxyribonucleotide of claim 482, wherein said chemical linkage comprises or includes an olefinic bond at the [delta-position] α -position relative to x, y or z, or any of the moieties:

$$-CH = CH_{2} - NH -$$

$$-CH = CH - CH_{2} - NH -$$

$$[-CH = CH - CH_{2} - O - CH_{2} - CH - NH -,$$

$$OH, \qquad]$$

$$-CH = CH - CH_{2} - O - CH_{2} - CH - CH_{2} - NH -,$$

$$OH, \qquad OH, \qquad OH,$$

494. (Amended) The oligo- or polydeoxyribonucleotide of claim 482, wherein Sig is selected from the group consisting of a ligand and a specific ligand binding protein [complexed with a binding protein therefor, and said binding protein is conjugated to ferritin].

504. (Amended) The composition of claim 502, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and [anti-Sig] anti-hapten immunoglobulin.

508. (Twice Amended) The oligo- or polydeoxyribonucleotide of claim 506, wherein both y and z of said terminal nucleotide comprise [a hydrogen] an oxygen atom at each of the 3' and 2' positions thereof, respectively.

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510. (Amended) The oligo- or polydexoyribonucleotide of claim 482, having the structural formula:

wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

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511. (Amended) An oligo- or [polyribonucleotide] polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one [ribonucleotide] modified nucleotide having the formula

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM [at a position of SM selected from the 2', 3' and 5' positions, or combinations thereof], said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig [being a moiety capable of non-radioactive detection] comprising a nonradioactive label mojety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or [polyribonucleotide] polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not [a cleaved 3' terminal ribonucleotide] obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said [oligo- or polyribonucleotide] oligoribonucleotide or polyribonucleotide.

512. (Amended) The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 511, wherein said Sig is or renders the nucleotide <u>or the oligo- or polynucleotide</u> self-signaling or self-indicating or self-detecting.

Claim 513, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 514, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 515, line 1, change "polyribonucleotide" to -- polynucleotide -- .

516. (Amended) The oligo- or [polyribonucleotide] polynucleotide of claim 511, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the [alpha-position] α-position relative to the point of attachment to the nucleotide, a -CH₂NH- moiety, or both.

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Claim 517, line 1, change "polyribonucleotide" to -- polynucleotide -- .

518. The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 511, wherein said chemical linkage comprises or includes an olefinic bond at the [delta-position] α <u>position</u> relative to the point of attachment to the nucleotide, or any of the moieties:

 $0 \\ | | \\ - S -, - C - O, and - O -$

Claim 519, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 520, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 521, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 522, line 1, change "polyribonucleotide" to -- polynucleotide -- .

523. (Amended) The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 511, wherein Sig is <u>selected from the group consisting of a ligand and a specific ligand binding protein</u> [complexed with a binding protein therefor, and said binding protein is conjugated to ferritin].

Claim 524, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 525, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 526, line 1, change "polyribonucleotide" to -- polynucleotide -- .

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Claim 527, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 528, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 529, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 530, lines 1 and 2, change "polyribonucleotide" to -- polynucleotide -- .

Claim 531, line 1, change "polyribonucleotide" to -- polynucleotide -- .

533. (Amended) The composition of claim 531, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and [anti-Sig] anti-hapten MIS immunoglobulin.

> 535. (Amended) The oligo- or [polyribonucleotide] polynucleotide of claim 511, wherein said Sig moiety is attached to a terminal [ribonucleotide] nucleotide in said oligo- or [polyribonucleotide] polynucleotide.

536. (Amended) The oligo- or [polyribonucleotide] polynucleotide of claim 535, MIG wherein the sugar moiety of said terminal [ribonucleotide] nucleotide has a hydrogen atom at the 2' position thereof.

> 537. (Amended) The oligo- or [polyribonucleotide] polynucleotide of claim 535, wherein the sugar moiety of said terminal nucleotide has [a hydrogen] an oxygen atom at each of the 2' and 3' positions thereof.

Claim 538, line 1, change "polyribonucleotide" to -- polynucleotide -- .

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539. (Amended) An oligo- or [polyribonucleotide] polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the structural formula:

wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H- , HO- , a monophosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H- , HO- , a monophosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H-, HO-, a mono-

phosphate, a di-phosphate and a tri-phosphate; and wherein Sig is covalently attached [to x, y or z] directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, and a combination thereof, said Sig [being a moiety capable of non-radioactive detection] comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to [x, y or z] said phosphate or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide and when Sig is attached through a chemical linkage to [y of] a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not [a cleaved 3' terminal ribonucleotide] obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said [oligo- or polyribonucleotide] oligoribonucleotide or

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polyribonucleotide.

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Claim 540, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 541, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 542, line 1, charge "polyribonucleotide" to -- polynucleotide -- .

Claim 543, line 1, change "polyribonucleotide" to -- polynucleotide -- .

544. (Amended) The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 539, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the [alpha-position] α -position relative to the point of attachment to the nucleotide, a -CH₂NH- moiety, or both.

Claim 545, line 1, change "polyribonucleotide" to -- polynucleotide -- .

546. (Amended) The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 539, wherein said chemical linkage comprises or includes an olefinic bond at the [delta-position] α -position relative to x, y or z, or any of the moieties:

$$- CH = CH_{2} - NH -$$

$$- CH = CH - CH_{2} - NH -$$

$$[- CH = CH - CH_{2} - O - CH_{2} - CH - NH -,$$

$$| OH, |]$$

$$- CH = CH - CH_{2} - O - CH_{2} - CH - CH_{2} - NH -,$$

$$| OH, | OH, | OH,$$

Claim 547, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 548, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 549, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 550, line 1, change "polyribonucleotide" to -- polynucleotide -- .

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551. (Amended) The oligo- or [polyribonucleotide] polynucleotide of claim 539, wherein Sig is selected from the group consisting of a ligand and a specific ligand binding protein [complexed with a binding protein therefor, and said binding protein is conjugated to ferritin].

Claim 552, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 553, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 554, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 555, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 556, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 557, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 558, lines 1 and 2, change "polyribonucleotide" to -- polynucleotide -- in both instances.

Claim 559, line 1, change "polyribonucleotide" to -- polynucleotide -- .

561. (Amended) The composition of claim 559, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and [anti-Sig] anti-hapten immunoglobulin.

Claim 563, lines 1 and 2, change "polyribonucleotide" to -- polynucleotide -- , both instances.

Claim 564, line 1, change "polyribonucleotide" to -- polynucleotide -- .

565. (Twice Amended) The oligo- or [polyribonucleotide] polynucleotide of claim 563, wherein both y and z of said terminal nucleotide comprise [a hydrogen] an oxygen atom at each of the 3' and 2' positions thereof, respectively.

Claim 566, line 1, change "polyribonucleotide" to -- polynucleotide -- .

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567. (Amended) The oligo- or [polydexoyribonucleotide] <u>polynucleotide</u> of claim 539, having the structural formula:

, wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

Cancel claims 568-575.

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